(FILE 'HOME' ENTERED AT 11:47:44 ON 09 JAN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, CABA' ENTERED AT 11:48:00 ON 09 JAN 2003

L1	25	S IRES AND PLANT AND EUKARYOT?
L2	16	DUP REMOVE L1 (9 DUPLICATES REMOVED)
L3	44	S IRES AND PLANT AND (ANIMAL OR MAMMAL OR INSECT)
L4	31	DUP REMOVE L3 (13 DUPLICATES REMOVED)

L4 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:927564 CAPLUS
TITLE: Artificial chromosome expression vectors containing elements of site-specific recombination systems for convenient integration of foreign genes
INVENTOR(S): Perkins, Edward; Perez, Carl; Lindenbaum, Michael; Greene, Amy; Leung, Josephine; Fleming, Elena; Stewart, Sandra; Shellard, Joan
PATENT ASSIGNEE(S): Chromos Molecular Systems, Inc., Can.
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097059	A2	20021205	WO 2002-US17452	20020530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-294758P P 20010530
US 2002-366891P P 20020321

AB Artificial chromosomes, including Aces (artificial chromosome expression systems), that have been engineered to contain sites for site-specific, integration of DNA of interest are provided. These artificial chromosomes permit tractable, efficient, rational engineering of the chromosome for a variety of applications. Construction of vectors and the development of lines carrying single copies of an integration site such as loxP or attB is described. Vectors carrying individual copies of several different integration sites is also described.

L4 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:315117 CAPLUS
DOCUMENT NUMBER: 136:336179
TITLE: Antibiotic-based gene regulation system in **plant** and mammalian cell responsive to streptogramins or tetracycline
INVENTOR(S): Fussenegger, Martin; Bailey, James E.
PATENT ASSIGNEE(S): Cistronics Cell Technology G.m.b.H., Switz.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002033104	A2	20020425	WO 2001-IB1963	20011019

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002010802 A5 20020429 AU 2002-10802 20011019
PRIORITY APPLN. INFO.: US 2000-693624 A 20001020
WO 2001-IB1963 W 20011019

AB The invention relates to a novel system for gene regulation in eukaryotic cells, and methods of using the same for protein prodn., tissue engineering and gene therapy. In particular, the invention provides a new system for antibiotic-regulated gene expression in eukaryotic cells based on sequences from Actinomycetes antibiotic resistance promoters, polypeptides that bind to the same in an antibiotic responsive manner, and nucleotides encoding such polypeptides. The new gene regulation system is responsive to streptogramins, such as pristinamycin and virginiamycin, and tetracycline. Further, the invention provides novel and sensitive methods of screening for candidate antibiotics. The streptogramin-based regulation system shows over 10-fold lower baseline expression level and up to 4- fold higher rations than TET-responsive system. More importantly, streptogramins and tetracycline regulate their resp. mammalian transcription systems essentially independently, showing that these two systems can be used together to achieve advanced therapeutic regimens in which to sets of transgene can be regulated sep.

L4 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220805 CAPLUS
DOCUMENT NUMBER: 136:242947
TITLE: Internal ribosome entry sites (**IRES**) of errantiviruses and uses in cap-independent mRNA translation
INVENTOR(S): Meignin, Carine; Vaury, Chantal
PATENT ASSIGNEE(S): Institut National de la Sante et de la Recherche Medicale (INSERM), Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022839	A2	20020321	WO 2001-IB2084	20010917
WO 2002022839	A3	20020516		

W: AU, CA, JP, NZ, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

AU 2002015499 A5 20020326 AU 2002-15499 20010917
PRIORITY APPLN. INFO.: EP 2000-402553 A 20000915
WO 2001-IB2084 W 20010917

AB The present invention relates to recombinant DNA mols. comprising an Internal Ribosome Entry Site (**IRES**), wherein said **IRES** is isolated from an errantivirus and controls cap-independent mRNA translation. More particularly, these **IRES** are isolated from the retroelements ZAM and Idemfix. The invention is also directed to expression vectors comprising said recombinant DNA mol. and their uses

thereof. The said expression vector comprises the sequences to be expressed encode polypeptides selected from polypeptides with therapeutic activities, poly ptides aimed at correcting defi encies due to mutated genes in a given organism, polypeptides able to inactivate genes assocd. with pathologies, polypeptides capable of inhibiting cellular functions, polypeptides that block cell proliferation, polypeptides as commodities, antibodies and fragments thereof and antigenes. The invention demonstrates that the 5'-UTR of ZAM and Idemfix display a segment able to initiate translation within a dicistronic construct and it may only require the canonical initiation factors necessary for translation and not addnl. trans-acting factors such as specific viral or host factors. When analyzed in vivo through a transgenic approach performed in Drosophila, Idenmfix **IRES** exhibits some degree of developmental regulation and it is active in third instar larval tissues where the translation of the first and the second cistron of the dicistronic transgenes are easily detected but its activity is absent in embryos whatever their developmental stage. The invention indicate that this **IRES** needs eukaryotic initiation factors independent from their host origin (Rabbit in RRL or Drosophila in vivo), and specific trans-acting factors that account for the cell-type differences in **IRES** function.

L4 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:556138 CAPLUS
DOCUMENT NUMBER: 137:104792
TITLE: Methods to overexpress a foreign gene in a cell or in an **animal** in vitro and in vivo
INVENTOR(S): Efstratiadis, Argiris; Ludwig, Thomas; Kljuic, Ana; Politi, Katerina
PATENT ASSIGNEE(S): The Trustees of Columbia University, USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002099194	A1	20020725	US 2001-905311	20010713

PRIORITY APPLN. INFO.: US 2000-218945P P 20000714
AB The present invention provides genetic constructs comprising: (a) a region of DNA which is homologous to a region of an endogenous gene present in a genome of a cell of interest; (b) a first nucleic acid encoding an encephalomyocarditis internal ribosome entry site (EMCV **IRES**); (c) a second nucleic acid encoding a selectable marker which can be excised from the nucleic acid mol. if the nucleic acid mol. has been integrated into the genome of the cell of interest; and (d) a third nucleic acid encoding a gene of interest. The invention is exemplified by generating polyomavirus midentifiedle T antigen (mT) overexpressing transgenic mice for the study of the signal transduction involved in tumorigenesis for breast cancer. Other members involved mT activated signaling pathways, like tyrosine kinase Shc or Akt1 are also selected to express in the mT activated transgenic mice. The cell may be an **animal** cell, a yeast cell or a **plant** cell. The invention also provides for transgenic non-human **animals** which are created using the above described construct. The invention also provides methods for making such transgenic **animals**.

L4 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:221167 CAPLUS
DOCUMENT NUMBER: 136:242919
TITLE: Methods for coexpression of two or more genes in eukaryotic cells by utilizing sequence of internal

ribosomal entry site derived from tobamovirus

INVENTOR(S): Atabekov, Joseph; Korpela, Tim[redacted]; Dorokhov, Yurii; Ivanov, Peter; Skulachev, Max[redacted]; Rodionova, Nina; Karpova, Olga

PATENT ASSIGNEE(S): Russia

SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 424,793.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002034814	A1	20020321	US 2001-911732	20010725
FI 9702293	A	19981201	FI 1997-2293	19970530
WO 9854342	A1	19981203	WO 1998-FI457	19980529

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6376745	B1	20020423	US 1999-424793	19991216

PRIORITY APPLN. INFO.:

FI 1997-2293	A	19970530
WO 1998-FI457	W	19980529
US 1999-424793	A2	19991216

AB The present invention discloses a primary object of this invention is to provide a method which will enable to coexpress simultaneously two (or more) desired genes in **plant**, **animal** or yeast cells, in transgenic **plants** and **animals**, or in vitro, in **plant** cell-derived or **animal** cell-derived translation systems by using sequence of internal ribosomal entry site derived from tobamovirus . In particular, the sequence elements are derived from RNAs of a tobamovirus upstream of MP gene or CP gene termed here as IRESmp and IREScp , resp. The method of this invention involves the construction of a recombinant nucleic acid sequence which comprises a specific transcriptional promoter, a first gene expressible in eukaryotic cells linked to said transcriptional promoter, IRESmp or IREScp located 3' to the first gene and a second gene expressible in eukaryotic cells, located 3' to **IRES** sequence such that the second gene is placed under the transcriptional control of **IRES** sequence originated from tobamovirus genome. The primary chimeric RNA transcript in pos. sense polarity is produced by the transformed cells from the said promoter. The expression of the first gene occurs by direct translation whereas the translation of the 5'-distal gene(s) of bicistronic (or polycistronic) mRNA will be promoted by IRESmp or IREScp .

L4 ANSWER 6 OF 31 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2002237335 MEDLINE

DOCUMENT NUMBER: 21957245 PubMed ID: 11959981

TITLE: Polypurine (A)-rich sequences promote cross-kingdom conservation of internal ribosome entry.

AUTHOR: Dorokhov Yuri L; Skulachev Maxim V; Ivanov Peter A; Zvereva Svetlana D; Tjulkina Lydia G; Merits Andres; Gleba Yuri Y; Hohn Thomas; Atabekov Joseph G

CORPORATE SOURCE: A. N. Belozersky Institute of Physico-Chemical Biology, Moscow State University, 119899 Moscow, Russia.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 Apr 16) 99 (8) 5301-6. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020429
Last Updated on STN: 20020615
Entered Medline: 20020614

AB The internal ribosome entry sites (**IRES**), **IRES** (CP,148)(CR) and **IRES**(MP,75)(CR), precede the coat protein (CP) and movement protein (MP) genes of crucifer-infecting tobamovirus (crTMV), respectively. In the present work, we analyzed the activity of these elements in transgenic **plants** and other organisms. Comparison of the relative activities of the crTMV **IRES** elements and the **IRES** from an **animal** virus--encephalomyocarditis virus--in **plant**, yeast, and HeLa cells identified the 148-nt **IRES**(CP,148)(CR) as the strongest element that also displayed **IRES** activity across all kingdoms. Deletion analysis suggested that the polypurine (A)-rich sequences (PARSs) contained in **IRES** (CP,148)(CR) are responsible for these features. On the basis of those findings, we designed artificial PARS-containing elements and showed that they, too, promote internal translation from dicistronic transcripts in vitro, in tobacco protoplasts and in HeLa cells. The maximum **IRES** activity was obtained from multiple copies of either (A)(4)G(A)(2)(G)(2) or G(A)(2-5) as contained in **IRES**(CP,148)(CR). Remarkably, even homopolymeric poly(A) was moderately active, whereas a poly(G) homopolymer was not active. Furthermore, a database search for existing PARS sequences in 5'-untranslated regions (5'UTR) of genes in tobacco genome allowed the easy identification of a number of **IRES** candidates, in particular in the 5'UTR of the gene encoding Nicotiana tabacum heat-shock factor 1 (NtHSF1). Consistent with our prediction, the 5'UTR of NtHSF1 turned out to be an **IRES** element active in vitro, in **plant** protoplasts and HeLa cells. We predict that PARS elements, when found in other mRNAs, will show a similar activity.

L4 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:796349 CAPLUS
TITLE: The biotechnological application and limitation of **IRES** to deliver multiple defence genes to **plant** pathogens
AUTHOR(S): Urwin, P. E.; Zubko, E. I.; Atkinson, H. J.
CORPORATE SOURCE: Centre for Plant Sciences, Leeds Institute for Plant Biotechnology and Agriculture, University of Leeds, Leeds, LS2 9JT, UK
SOURCE: Physiological and Molecular Plant Pathology (2002), 61(2), 103-108
CODEN: PMPPEZ; ISSN: 0885-5765
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Transgenic resistance often has enhanced efficacy when more than one transgene is expressed. Here, we explore the co-delivery of multiple discrete effectors via a single transgene using an internal ribosome entry site (**IRES**) sequence. As an example, we report the co-delivery of two distinct proteinase inhibitors in Nicotiana tabacum var. Xanthi from a bicistronic **plant** mRNA to examine resistance against **plant** parasitic nematodes. A cysteine proteinase inhibitor, Oc-I.DELTA.D86, is translated in a normal cap-dependent manner while translation of the serine proteinase inhibitor, CpTI, from the bicistronic mRNA is **IRES**-mediated. ELISAs using antibodies confirm the expression of the two inhibitors in aerial and root material and suggest

that **IRES**-mediated expression in the roots is lower than normal cap-dependent expression. Anal. of Globodera tabacum recovered from transgenic Nicotiana expressing two discrete protease inhibitors revealed appreciable levels of resistance of up to 51 .+-. 3%. Histochem. anal. of **animals** recovered from transgenic Nicotiana lines expressing Oc-I.DELTA.D86, via cap-dependent translation revealed a marked redn. in cysteine proteolytic activity in comparison to those from control untransformed **plants**. A less dramatic redn. was obsd. in similar anal. of serine proteolytic activity of **animals** recovered from transgenic Nicotiana lines expressing CpTI via **IRES** -mediated translation. The utility of using an **IRES** element to deliver a no. of discrete anti-pathogen proteins is discussed.

L4 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:636090 CAPLUS
DOCUMENT NUMBER: 135:206449
TITLE: Gene expression system based on chimeric steroid/thyroid hormone receptors and uses in modulating target gene expression
INVENTOR(S): Gage, Fred H.; Suhr, Steven T.
PATENT ASSIGNEE(S): Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062780	A1	20010830	WO 2001-US5750	20010223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1259537	A1	20021127	EP 2001-912956	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-184591P P 20000224
WO 2001-US5750 W 20010223

AB The invention provides a system for modulating the expression of a target gene in a subject wherein a defined response element for a DNA binding domain modulates expression of the target gene. The invented system comprises two chimeric proteins, each contg. the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily, one of which is non-endogenous to the subject. In addn., the first chimeric protein contains a DNA binding domain to which the target gene is responsive and the second chimeric protein contains a transcription modulating domain, such as a transcription activator or a transcription repressor. Two of the invention systems form a dimer having the properties of a native heterodimer or homodimer, and only the first chimeric protein contains a DNA binding domain and only the second chimeric protein contains a transcription activating domain. The functional entity formed by assocn. of the first and second chimeric proteins can be designed to transactivate transcription by complexing with a DNA binding recognition site that does not have the 2-half site format

common to response elements for members of the steroid/thyroid hormone nuclear receptor superfamily. Thus, certain of the invention systems cannot functionally interact with endogenous proteins in the way that wild
type receptors do. The invention further provides DNA sequences encoding the invention chimeric proteins, cells contg. such DNA sequences, and methods for using the invention chimeric proteins to modulate expression of one or more non-endogenous genes in a subject organism.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:598202 CAPLUS
DOCUMENT NUMBER: 135:191286
TITLE: Initiation of cap independent translation in **plant** using stress-induced **IRES** element from the leader of Arabidopsis RPS18C gene
INVENTOR(S): Vanderhaeghen, Rudy; Van Lijsebettens, Maria
PATENT ASSIGNEE(S): Vlaams Interuniversitair Instituut Voor Biotechnologie
Vzw, Belg.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059138	A2	20010816	WO 2001-EP1026	20010201
WO 2001059138	A3	20020221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1261728	A2	20021204	EP 2001-915180	20010201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: EP 2000-200442 A 20000210
WO 2001-EP1026 W 20010201

AB The present invention relates to a new sequence derived from a **plant** gene, capable of initiating cap independent translation in eukaryotic cells, particularly in **plants**. Surprisingly, it was found that the leader sequence of RPS18C, belonging to the Arabidopsis RPS18 gene family, was contg. an **IRES** sequence and can initiate cap independent translation. Cap independent ribosome recognition was triggered by base-pairing of a 5'-UTR oligopyrimidine tract to the 3'-end of the 18S rRNA. This sequence contains a motif that is similar to the "box A" (UUUCC element) of picornaviral IRESs. The cap independent translation can be inhibited by the sequence which is complementary to the
3' end of the 18S rRNA. Said cap independent translation is active- and induced under stress conditions, preferably salt stress and/or general starvation. Such cap-independent initiation of translation and subsequent
translation can be used to create a dicistronic and/or oligocistronic expression systems.

L4 ANSWER 10 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:557512 BIOSIS
DOCUMENT NUMBER: PREV200100557512
TITLE: [redacted]ernal initiation in Saccharomyc[redacted] cerevisiae mediated by an initiator tRNA/eIF2-independent internal ribosome entry site element.
AUTHOR(S): Thompson, Sunnie R.; Gulyas, Keith D.; Sarnow, Peter (1)
CORPORATE SOURCE: (1) Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA, 94305: psarnow@stanford.edu USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (Nobember 6, 2001) Vol. 98, No. 23, pp. 12972-12977. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Internal initiation of translation can be mediated by specific internal ribosome entry site (**IRES**) elements that are located in certain mammalian and viral mRNA molecules. Thus far, these mammalian cellular and viral **IRES** elements have not been shown to function in the yeast Saccharomyces cerevisiae. We report here that a recently discovered **IRES** located in the genome of cricket paralysis virus can direct the efficient translation of a second URA3 cistron in dicistronic mRNAs in S. cerevisiae, thereby conferring uracil-independent growth. Curiously, the **IRES** functions poorly in wild-type yeast but functions efficiently either in the presence of constitutive expression of the eIF2 kinase GCN2 or in cells that have two initiator tRNAmet genes disrupted. Both of these conditions have been shown to lower the amounts of ternary eIF2-GTP/initiator tRNAmet complexes. Furthermore, tRNAmet-independent initiation was also observed in translation-competent extracts prepared from S. cerevisiae in the presence of edeine, a compound that has been shown to interfere with start codon recognition by ribosomal subunits carrying ternary complexes. Therefore, the cricket paralysis virus **IRES** is likely to recruit ribosomes by internal initiation in S. cerevisiae in the absence of eIF2 and initiator tRNAmet, by the same mechanism of factor-independent ribosome recruitment used in mammalian cells. These findings will allow the use of yeast genetics to determine the mechanism of internal ribosome entry.

L4 ANSWER 11 OF 31 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001534416 MEDLINE
DOCUMENT NUMBER: 21465047 PubMed ID: 11581392
TITLE: The 5' untranslated region of Rhopalosiphum padi virus contains an internal ribosome entry site which functions efficiently in mammalian, **plant**, and **insect** translation systems.
AUTHOR: Woolaway K E; Lazaridis K; Belsham G J; Carter M J; Roberts L O
CORPORATE SOURCE: School of Biomedical and Life Sciences, University of Surrey, Guildford GU2 7XH, United Kingdom.
SOURCE: JOURNAL OF VIROLOGY, (2001 Nov) 75 (21) 10244-9.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011003
Last Updated on STN: 20011029
Entered Medline: 20011025

AB Rhopalosiphum padi virus (RhPV) is one of several picorna-like viruses that infect **insects**; sequence analysis has revealed distinct

differences between these agents and mammalian picornaviruses. RhPV has a single-stranded positive-sense RNA genome of about 10 kb; unlike the genomes of Picornaviridae, however, this genome contains two long open reading frames (ORFs). ORF1 encodes the virus nonstructural proteins, while the downstream ORF, ORF2, specifies the structural proteins. Both ORFs are preceded by long untranslated regions (UTRs). The intergenic UTR is known to contain an internal ribosome entry site (**IRES**) which directs non-AUG-initiated translation of ORF2. We have examined the 5' UTR of RhPV for **IRES** activity by translating synthetic dicistronic mRNAs containing this sequence in a variety of systems. We now report that the 5' UTR contains an element which directs internal initiation of protein synthesis from an AUG codon in mammalian, **plant**, and Drosophila in vitro translation systems. In contrast, the encephalomyocarditis virus **IRES** functions only in the mammalian system. The RhPV 5' **IRES** element has features in common with picornavirus **IRES** elements, in that no coding sequence is required for **IRES** function, but also with cellular **IRES** elements, as deletion analysis indicates that this **IRES** element does not have sharply defined boundaries.

L4 ANSWER 12 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:354604 BIOSIS
DOCUMENT NUMBER: PREV200100354604
TITLE: Molecular mechanisms of translation initiation in eukaryotes.
AUTHOR(S): Pestova, Tatyana V.; Kolupaeva, Victoria G.; Lomakin, Ivan B.; Pilipenko, Evgeny V.; Shatsky, Ivan N.; Agol, Vadim I.; Hellen, Christopher U. T. (1)
CORPORATE SOURCE: (1) Department of Microbiology and Immunology, State University of New York Health Science Center at Brooklyn, 450 Clarkson Avenue, Brooklyn, NY, 11203: chellen@netmail.hscbkyn.edu USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (June 19, 2001) Vol. 98, No. 13, pp. 7029-7036. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Translation initiation is a complex process in which initiator tRNA, 40S, and 60S ribosomal subunits are assembled by eukaryotic initiation factors (eIFs) into an 80S ribosome at the initiation codon of mRNA. The cap-binding complex eIF4F and the factors eIF4A and eIF4B are required for binding of 43S complexes (comprising a 40S subunit, eIF2/GTP/Met-tRNAi and eIF3) to the 5' end of capped mRNA but are not sufficient to promote ribosomal scanning to the initiation codon. eIF1A enhances the ability of eIF1 to dissociate aberrantly assembled complexes from mRNA, and these factors synergistically mediate 48S complex assembly at the initiation codon. Joining of 48S complexes to 60S subunits to form 80S ribosomes requires eIF5B, which has an essential ribosome-dependent GTPase activity and hydrolysis of eIF2-bound GTP induced by eIF5. Initiation on a few mRNAs is cap-independent and occurs instead by internal ribosomal entry. Encephalomyocarditis virus (EMCV) and hepatitis C virus epitomize distinct mechanisms of internal ribosomal entry site (**IRES**)-mediated initiation. The eIF4A and eIF4G subunits of eIF4F bind immediately upstream of the EMCV initiation codon and promote binding of 43S complexes. EMCV initiation does not involve scanning and does not require eIF1, eIF1A, and the eIF4E subunit of eIF4F. Initiation on some EMCV-like IRESs requires additional noncanonical initiation factors, which alter **IRES** conformation and promote binding of eIF4A/4G. Initiation on

the hepatitis C virus **IRES** is even simpler: 43S complexes containing only eIF2 and eIF3 bind directly to the initiation codon as a result of specific interaction of the **IRES** and the 40S subunit.

L4 ANSWER 13 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:226690 BIOSIS
DOCUMENT NUMBER: PREV200200226690
TITLE: Irresistible **IRES**. Attracting the translation machinery to internal ribosome entry sites.
AUTHOR(S): Vagner, Stephan (1); Galy, Bruno; Pyronnet, Stephane
CORPORATE SOURCE: (1) INSERM U397, Institut Louis Bugnard, CHU Rangueil, 31403, Toulouse: vagner@rangueil.inserm.fr France
SOURCE: EMBO Reports, (October, 2001) Vol. 2, No. 10, pp. 893-898. http://www.embo-reports.oupjournals.org. print. ISSN: 1469-221X.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Studies on the control of eukaryotic translation initiation by a cap-independent recruitment of the 40S ribosomal subunit to internal messenger RNA sequences called internal ribosome entry sites (IRESs) have shown that these sequence elements are present in a growing list of viral and cellular RNAs. Here we discuss their prevalence, mechanisms whereby they may function and their uses in regulating gene expression.

L4 ANSWER 14 OF 31 MEDLINE
ACCESSION NUMBER: 2000325323 MEDLINE
DOCUMENT NUMBER: 20325323 PubMed ID: 10866656
TITLE: Naturally occurring dicistronic cricket paralysis virus RNA is regulated by two internal ribosome entry sites.
AUTHOR: Wilson J E; Powell M J; Hoover S E; Sarnow P
CORPORATE SOURCE: Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, California 94305, USA.
CONTRACT NUMBER: R01 AI 25105 (NIAID)
R01 GM55979 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (2000 Jul) 20 (14) 4990-9. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF218039
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000724
AB Cricket paralysis virus is a member of a group of **insect** picorna-like viruses. Cloning and sequencing of the single plus-strand RNA genome revealed the presence of two nonoverlapping open reading frames, ORF1 and ORF2, that encode the nonstructural and structural proteins, respectively. We show that each ORF is preceded by one internal ribosome entry site (**IRES**). The intergenic **IRES** is located 6,024 nucleotides from the 5' end of the viral RNA and is more active than the **IRES** located at the 5' end of the RNA, providing a mechanistic explanation for the increased abundance of structural proteins relative to nonstructural proteins in infected cells. Mutational analysis of this intergenic-region **IRES** revealed that ORF2 begins with a noncognate CCU triplet. Complementarity of this CCU triplet with sequences in the **IRES** is important for **IRES** function, pointing to an involvement of RNA-RNA interactions in translation initiation. Thus,

SOURCE: GENE EXPRESSION, (2000) 9 (3) 133-43.
Journal code: 9200651. ISSN: 1052-2166.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB The gamma-monomethylphosphate cap structure is found in several eukaryotic small RNAs including nuclear U6, U6atac, 7SK, **plant** nucleolar U3, and rodent cytoplasmic B2 RNAs. In the case of human U6 snRNA, the 5' end sequence corresponding to nucleotides 1-25 serves as the capping signal and directs the formation of methylphosphate cap structure. In this study, we show that the U6 RNA capping signal, when introduced at the 5' end of RNAs, can efficiently direct the methylphosphate cap formation in RNAs of up to 2.7 kb long, as well as in different mRNAs. These data show that the methylphosphate capping signal functions in mRNAs having different primary sequences and different lengths. Presence of the methylphosphate cap structure on the 5' end of a luciferase mRNA with EMCV 5' noncoding region, which is translated in an **IRES**-dependent pathway, resulted in a 6- to 100-fold inhibition of translation compared to the same mRNA with a 5' triphosphate when microinjected into frog oocytes or expressed in mouse cells in tissue culture. Thus, conversion of the pppG structure to a methyl-pppG structure on the 5' end of an mRNA, which is translated in an **IRES**-dependent pathway, results in severe inhibition of translation. These data show that the 5' end motif of mRNAs plays an important role even in the **IRES**-mediated mRNA translation.

L4 ANSWER 17 OF 31 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999107899 MEDLINE
DOCUMENT NUMBER: 99107899 PubMed ID: 9891009
TITLE: Molecular cloning of mouse glycolate oxidase. High evolutionary conservation and presence of an iron-responsive element-like sequence in the mRNA.
COMMENT: Erratum in: J Biol Chem 1999 May 28;274(22):15966
AUTHOR: Kohler S A; Menotti E; Kuhn L C
CORPORATE SOURCE: Swiss Institute for Experimental Cancer Research, CH-1066 Epalinges s/Lausanne, Switzerland.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Jan 22) 274 (4) 2401-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF104312
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 20021218
Entered Medline: 19990216

AB Iron regulatory proteins (IRPs) control the synthesis of several proteins in iron metabolism by binding to iron-responsive elements (**IREs**), a hairpin structure in the untranslated region (UTR) of corresponding mRNAs. Binding of IRPs to **IREs** in the 5' UTR inhibits translation of ferritin heavy and light chain, erythroid aminolevulinic acid synthase, mitochondrial aconitase, and Drosophila succinate dehydrogenase b, whereas IRP binding to **IREs** in the 3' UTR of transferrin receptor mRNA prolongs mRNA half-life. To identify new targets

of IRPs, we devised a method to enrich IRE-containing mRNAs by using recombinant IRP-1 as an affinity matrix. A cDNA library established from enriched mRNA was screened by an RNA-protein band shift assay. This revealed a novel IRE-like sequence in the 3' UTR of a liver-specific mouse mRNA. The newly identified cDNA codes for a protein with high homology to **plant** glycolate oxidase (GOX). Recombinant protein expressed in bacteria displayed enzymatic GOX activity. Therefore, this cDNA represents the first vertebrate GOX homologue. The IRE-like sequence in mouse GOX exhibited strong binding to IRPs at room temperature. However, it differs from functional **IREs** by a mismatch in the middle of its upper stem and did not confer iron-dependent regulation in cells.

L4 ANSWER 18 OF 31 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000084623 MEDLINE
DOCUMENT NUMBER: 20084623 PubMed ID: 10619605
TITLE: Organization of the ferritin genes in Drosophila melanogaster.
AUTHOR: Dunkov B C; Georgieva T
CORPORATE SOURCE: Department of Biochemistry and the Center for Insect Science, University of Arizona, Tuscon 85721, USA.. dunkov@u.arizona.edu
SOURCE: DNA AND CELL BIOLOGY, (1999 Dec) 18 (12) 937-44. Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF145125; GENBANK-AF145126
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB The organization of two closely clustered genes, Fer1HCH and Fer2LCH, encoding the heavy-chain homolog (HCH) and the light-chain homolog (LCH) subunits of Drosophila melanogaster ferritin are reported here. The 5019-bp sequence of the cluster was assembled from genomic fragments obtained by polymerase chain reaction (PCR) amplification of genomic DNA and from sequences obtained from the Berkeley Drosophila Genome Project (BDGP) (http://www.fruitfly.org). These genes, located at position 99F1, have different exon-intron structures (Fer1HCH has three introns and Fer2LCH has two introns) and are divergently transcribed. Computer analysis of the possibly shared promoter regions revealed the presence of putative metal regulatory elements (MREs), a finding consistent with the upregulation of these genes by iron, and putative NF-kappaB-like binding sites. The structure of two other invertebrate ferritin genes, from the nematode Caenorhabditis elegans (located on chromosomes I and V), was also analyzed. Both nematode genes have two introns, lack iron-responsive elements (**IREs**), and encode ferritin subunits similar to vertebrate H chains. These findings, along with comparisons of ferritin genes from invertebrates, vertebrates, and **plants**, suggest that the specialization of ferritin H and L type chains, the complex exon-intron organization of **plant** and vertebrate genes, and the use of the IRE/iron regulatory protein (IRP) mechanism for regulation of ferritin synthesis are recent evolutionary acquisitions.

L4 ANSWER 19 OF 31 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999078017 MEDLINE
DOCUMENT NUMBER: 99078017 PubMed ID: 9858603
TITLE: Ribosomal pausing and scanning arrest as mechanisms of translational regulation from cap-distal iron-responsive elements.
AUTHOR: Paraskeva E; Gray N K; Schlager B; Wehr K; Hentze M W
CORPORATE SOURCE: European Molecular Biology Laboratory, D-69117 Heidelberg,

Germany.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1999 Jan) 19 (1) 807-16.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 20021218
Entered Medline: 19990210

AB Iron regulatory protein 1 (IRP-1) binding to an iron-responsive element (IRE) located close to the cap structure of mRNAs represses translation by precluding the recruitment of the small ribosomal subunit to these mRNAs. This mechanism is position dependent; reporter mRNAs bearing **IREs** located further downstream exhibit diminished translational control in transfected mammalian cells. To investigate the underlying mechanism, we have recapitulated this position effect in a rabbit reticulocyte cell-free translation system. We show that the recruitment of the 43S preinitiation complex to the mRNA is unaffected when IRP-1 is bound to a cap-distal IRE. Following 43S complex recruitment, the translation initiation apparatus appears to stall, before linearly progressing to the initiation codon. The slow passive dissociation rate of IRP-1 from the cap-distal IRE suggests that the mammalian translation apparatus plays an active role in overcoming the cap-distal IRE-IRP-1 complex. In contrast, cap-distal IRE-IRP-1 complexes efficiently repress translation in wheat germ and yeast translation extracts. Since inhibition occurs subsequent to 43S complex recruitment, an efficient arrest of productive scanning may represent a second mechanism by which RNA-protein interactions within the 5' untranslated region of an mRNA can regulate translation. In contrast to initiating ribosomes, elongating ribosomes from **mammal**, **plant**, and yeast cells are unaffected by IRE-IRP-1 complexes positioned within the open reading frame. These data shed light on a characteristic aspect of the IRE-IRP regulatory system and uncover properties of the initiation and elongation translation apparatus of eukaryotic cells.

L4 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:795149 CAPLUS
DOCUMENT NUMBER: 130:33987
TITLE: Coexpression of multiple genes in transgenic **plants** using tobamovirus internal ribosome entry sites
INVENTOR(S): Atabekov, Joseph; Korpela, Timo; Dorokhov, Yurii; Ivanov, Peter; Skulachev, Maxim; Rodionova, Nina; Karpova, Olga
PATENT ASSIGNEE(S): Russia
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854342	A1	19981203	WO 1998-FI457	19980529

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG

FI 9702293	A	19981201	FI 1997-2293	19970530
AU 9875339	A1	19981230	AU 1998-75339	19980529
EP 1017834	A1	20000712	EP 1998-922843	19980529
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514086	T2	20020514	JP 1999-500300	19980529
US 6376745	B1	20020423	US 1999-424793	19991216
US 2002034814	A1	20020321	US 2001-911732	20010725

PRIORITY APPLN. INFO.:
FI 1997-2293 A 19970530
WO 1998-FI457 W 19980529
US 1999-424793 A2 19991216

AB A primary object of this invention is to provide a method to allow simultaneous expression of desired genes in vitro and in planta. This object is accomplished by utilizing crucifer tobamovirus RNA sequences upstream of the MP gene (IRESmp). The method of this invention involves construction of a recombinant DNA mol. which comprises a promoter, a first **plant**-expressible gene linked to the promoter, IRESmp located 3' to the first gene and a second **plant**-expressible gene located 3' to the IRESmp such that the second gene is placed under the translational control of IRESmp. The primary chimeric continuous RNA transcript in pos. sense polarity is produced by the transformed cells from the **plant**-expressible promoter. The expression of the first gene takes place by direct translation of the 5'-proximal gene of this mRNA but the translation of the 5'-distal gene of the dicistronic mRNA will be promoted by IRESmp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:344498 CAPLUS
DOCUMENT NUMBER: 129:24155
TITLE: Method for identifying translationally regulated genes
INVENTOR(S): Luria, Sylvie; Einat, Paz; Harris, Nicholas; Skaliter, Rami; Grosman, Zehava
PATENT ASSIGNEE(S): QBI Enterprises Ltd., Israel; Kohn, Kenneth, I.; Luria, Sylvie; Einat, Paz; Harris, Nicholas; Skaliter, Rami; Grosman, Zehava
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821321	A1	19980522	WO 1997-US20831	19971112

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

GN, ML, MR, NE, SN, TD, TG

US 6013437	A	20000111	US 1996-748130	19961112
AU 9852580	A1	19980603	AU 1998-525[redacted]	19971112
EP 942969	A1	19990922	EP 1997-947522	19971112
R: AT, BE, CH, DE, FR, GB, IT, LI, LU				
JP 2002515754	T2	20020528	JP 1998-522854	19971112

PRIORITY APPLN. INFO.:

US 1996-748130	A	19961112
US 1997-943586	A	19971003
WO 1997-US20831	W	19971112

AB A method for identifying translationally regulated genes includes selectively stimulating translation of an unknown target mRNA using a stress-inducing factor wherein the target mRNA is part of a larger sample of mRNA. The mRNA sample is divided into pools of translated and untranslated mRNA (e.g., polysomal and nonpolysomal mRNA) which are differentially analyzed to identify genes that are translationally regulated by the stress inducing element. A method for identifying gene sequences coding for internal ribosome entry sites includes inhibiting 5'cap-dependent mRNA translation in a cell, collecting a pool of mRNA from the cells, and differentially analyzing the pool of mRNA to identify genes with sequences coding for internal ribosome entry sites. One method of inhibiting 5'cap-dependent mRNA translation is by expression of poliovirus 2A protease, which cleaves and inactivates eIF-4.gamma.. Application of the method to identification of genes regulated by oxygen deprivation or by heat stress was demonstrated. By sepn. of mRNA into polysomal and nonpolysomal fractions followed by differential display techniques or by differential expression anal. resulted in identification of many genes which could not be identified when total mRNA populations were compared.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:448123 BIOSIS
DOCUMENT NUMBER: PREV199800448123
TITLE: Loops and bulge/loops in iron-responsive element isoforms influence iron regulatory protein binding: Fine-tuning of mRNA regulation.
AUTHOR(S): Ke, Yaohuang; Wu, Jingyang; Leibold, Elizabeth A.; Walden, William E.; Theil, Elizabeth C. (1)
CORPORATE SOURCE: (1) Child. Hosp. Oakland, Res. Inst., 747 Fifty Second St., Oakland, CA 94609-1809 USA
SOURCE: Journal of Biological Chemistry, (Sept. 11, 1998) Vol. 273, No. 37, pp. 23637-23640.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

AB A family of noncoding mRNA sequences, iron-responsive elements (**IREs**), coordinately regulate several mRNAs through binding a family of mRNA-specific proteins, iron regulatory proteins (IRPs). **IREs** are hairpins with a constant terminal loop and base-paired stems interrupted by an internal loop/bulge (in ferritin mRNA) or a C-bulge (in m-aconitase, erythroid aminolevulinate synthase, and transferrin receptor mRNAs). IRP2 binding requires the conserved C-G base pair in the terminal loop, whereas IRP1 binding occurs with the C-G or engineered U-A. Here we show the contribution of the IRE internal loop/bulge to IRP2 binding by comparing natural and engineered IRE variants. Conversion of the internal loop/bulge in the ferritin-IRE to a C-bulge, by deletion of U, decreased IRP2 binding by > 95%, whereas IRP1 binding changed only 13%. Moreover, IRP2 binding to natural **IREs** with the C0bulge was similar to the DELTAU6 ferritin-IRE:>90% lover that the ferritin-IRE. The results predict mRNA-specific variation in

IRE-dependent regulation in vivo and may relate to previously observed differences in iron-induced ferritin and m-aconitase synthesis in liver and cultured cells. Variations in IRE structure and cellular IRP1/IRP2 ratios can provide a range of finely tuned, mRNA-specific responses to the same (iron) signal.

L4 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:67935 CAPLUS
DOCUMENT NUMBER: 128:214478
TITLE: The iron responsive element (IRE) family of mRNA regulators; regulation of iron transport and uptake compared in **animals**, **plants**, and microorganisms
AUTHOR(S): Theil, Elizabeth C.
CORPORATE SOURCE: Department of Biochemistry, North Carolina State University, Raleigh, NC, 27695-7622, USA
SOURCE: Metal Ions in Biological Systems (1998), 35, 403-434
CODEN: MIBSCD; ISSN: 0161-5149
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 124 refs., of the role of conserved mRNA sequences, the **IREs** (iron-responsive elements). Topics include structure and function of iso-**IREs** in regulating mRNA translation, stability, and turnover, proteins recognized by **IREs**, and comparison of regulation of iron uptake and storage in **animals**, **plants**, and microorganisms.

L4 ANSWER 24 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:222614 BIOSIS
DOCUMENT NUMBER: PREV199800222614
TITLE: Polypyrimidine tract-binding protein interacts with HnRNP L.
AUTHOR(S): Hahm, Bumsuk; Cho, Ook H.; Kim, Jung-E.; Kim, Yoon K.; Kim, Jong H.; Oh, Young L.; Jang, Sung K. (1)
CORPORATE SOURCE: (1) Dep. Life Sci., Pohang Univ. Sci. Technol., San31, Hyoja-Dong, Pohang, Kyungbuk 790-784 South Korea
SOURCE: FEBS Letters, (April 3, 1998) Vol. 425, No. 3, pp. 401-406.
ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Polypyrimidine tract-binding protein (PTB) is involved in pre-mRNA splicing and internal ribosomal entry site (**IRES**)-dependent translation. In order to identify cellular protein(s) interacting with PTB, we performed a yeast two-hybrid screening. Heterogeneous nuclear ribonucleoprotein L (hnRNP L) was identified as a PTB-binding protein. The interaction between PTB and hnRNP L was confirmed in an in vitro binding assay. Both PTB and hnRNP L were found to localize in the nucleoplasm, excepting the nucleoli, in HeLa cells by the green fluorescent protein (GFP)-fused protein detection method. The N-terminal half of PTB (aa 1-329) and most of hnRNP L (aa 141-558) is required for the interaction between PTB and hnRNP L.

L4 ANSWER 25 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:49846 BIOSIS
DOCUMENT NUMBER: PREV199900049846
TITLE: Inhibition of internal entry site (**IRES**)-mediated translation by a small yeast RNA: A novel strategy to block hepatitis C virus protein synthesis.
AUTHOR(S): Das, Saumitra; Ott, Michael; Yamane, Akemi; Venkatesan, Arun; Gupta, Sanjeev; Dasgupta, Asim (1)

CORPORATE SOURCE: (1) Dep. Microbiol. Immunol. and Mol. Genet., UCLA Sch. Med., Los Angeles, CA 90095-1747 USA
SOURCE: Frontiers in Bioscience, (Dec. 1, 1998) Vol. 3, No. CITED DEC. 16, 1998, pp. D250-268.
http://www.bioscience.org/1998/v3/d/das/d1252.htm.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB The observation that poliovirus mRNA is not translated in the yeast Saccharomyces cerevisiae has led to the discovery of a small RNA (60 nt, called IRNA, inhibitor RNA) which was later shown to specifically inhibit internal ribosome entry site (**IRES**)-mediated translation of naturally uncapped mRNAs. Translation of cellular capped mRNAs was not significantly inhibited by IRNA. IRNA also specifically inhibited hepatitis C virus (HCV) **IRES**-mediated translation in vitro and in vivo. A hepatoma cell line constitutively expressing IRNA was refractory to infection by a chimeric poliovirus (PV/HCV) in which PV **IRES** is replaced by HCV-**IRES**. In contrast, a PV/EMCV chimeric virus containing the EMCV **IRES** was not significantly inhibited in the IRNA-hepatoma cell line compared to the control hepatoma cells. UV-crosslinking studies showed that the IRNA binds a number of cellular proteins that appear to be important for **IRES**-mediated translation. Interaction of these proteins with the viral **IRES** elements is believed to be important in recruiting ribosomes to the 5'UTR of viral RNAs. The binding of the purified La autoantigen to the HCV **IRES** element was efficiently and specifically competed by IRNA. These results provide a basis for development of novel drugs effective against HCV infection.

L4 ANSWER 26 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:514736 BIOSIS
DOCUMENT NUMBER: PREV199799813939
TITLE: A dicistronic construct allows easy detection of human CFTR expression from YAC DNA in human cells.
AUTHOR(S): Vassaux, Georges (1); Huxley, Clare
CORPORATE SOURCE: (1) Dep. Biochem. and Molecular Genetics, Imperial Coll. Sch. Med., at St. Mary's, Norfolk Place, London W2 1PG UK
SOURCE: Nucleic Acids Research, (1997) Vol. 25, No. 20, pp. 4167-4168.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We have made a dicistronic construct where the picornaviral internal ribosome-entry site (**IRES**) driving the expression of the beta-geo gene has been inserted into the 3' untranslated region of the human CFTR gene present in a YAC. When introduced into the human cell line Caco-2 expressing the CFTR gene, the expression of the dicistronic gene can be detected by lacZ staining and follows the accumulation of the endogenous CFTR mRNA upon differentiation of the cells. These data demonstrate that this **IRES**-based approach presents an alternative to mRNA in situ hybridisation and allows detection of expression in an autologous system.

L4 ANSWER 27 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:154793 BIOSIS
DOCUMENT NUMBER: PREV199698726928
TITLE: Sequences within a small yeast RNA required for inhibition of internal initiation of translation: Interaction with La and other cellular proteins influences its inhibitory activity.
AUTHOR(S): Das, Saumitra; Kenan, Daniel J.; Bocskai, Diana; Keene, Jack D.; Dasgupta, Asim (1)
CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., UCLA Sch. Medicine, Los Angeles, CA 90024-1747 USA

SOURCE: Journal of Virology, (1996) Vol. 70, No. 3, pp. 1624-1632.
ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB We recently reported purification, determination of the nucleotide sequence, and cloning of a 60-nucleotide RNA (I-RNA) from the yeast Saccharomyces cerevisiae which preferentially blocked cap-independent, internal ribosome entry site (**IRES**)-mediated translation programmed by the poliovirus (PV) 5' untranslated region (UTR). The I-RNA appeared to inhibit **IRES**-mediated translation by virtue of its ability to bind a 52-kDa polypeptide which interacts with the 5' UTR of viral RNA. We demonstrate here that the HeLa 52-kDa I-RNA-binding protein is immunologically identical to human La autoantigen. Moreover, I-RNA-mediated inhibition of PV 5' UTR-dependent translation in cell extracts can be reversed by exogenous addition of purified La protein. By using I-RNAs with defined deletions, we have identified sequences of I-RNA required for inhibition of internal initiation of translation. Two smaller fragments of I-RNA (16 and 25 nucleotides) inhibited PV UTR-mediated translation from both monocistronic and bicistronic RNAs. When transfected into HeLa cells, these derivatives of I-RNA inhibited translation of PV RNA. A comparison of protein binding by active and inactive I-RNA mutants demonstrates that in addition to the La protein, three other polypeptides with apparent molecular masses of 80, 70, and 37 kDa may influence the translation-inhibitory activity of I-RNA.

L4 ANSWER 28 OF 31 MEDLINE
ACCESSION NUMBER: 96332624 MEDLINE
DOCUMENT NUMBER: 96332624 PubMed ID: 8695634
TITLE: The ferritins: molecular properties, iron storage function and cellular regulation.
AUTHOR: Harrison P M; Arosio P
CORPORATE SOURCE: Krebs Institute, Department of Molecular Biology and Biotechnology, University of Sheffield, UK.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Jul 31) 1275 (3) 161-203. Ref: 477
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19970203
Entered Medline: 19960905

AB The iron storage protein, ferritin, plays a key role in iron metabolism. Its ability to sequester the element gives ferritin the dual functions of iron detoxification and iron reserve. The importance of these functions is emphasised by ferritin's ubiquitous distribution among living species. Ferritin's three-dimensional structure is highly conserved. All ferritins have 24 protein subunits arranged in 432 symmetry to give a hollow shell with an 80 A diameter cavity capable of storing up to 4500 Fe(III) atoms as an inorganic complex. Subunits are folded as 4-helix bundles each having a fifth short helix at roughly 60 degrees to the bundle axis. Structural features of ferritins from humans, horse, bullfrog and bacteria are described: all have essentially the same architecture in spite of large variations in primary structure (amino acid sequence identities can be as low as 14%) and the presence in some bacterial ferritins of haem groups. Ferritin molecules isolated from vertebrates are composed of two

types of subunit (H and L), whereas those from **plants** and bacteria contain only H-type chains, where 'H-type' is associated with the presence of centres catalysing the oxidation of two Fe(II) atoms. The similarity between the dinuclear iron centres of ferritin H-chains and those of ribonucleotide reductase and other proteins suggests a possible wider evolutionary linkage. A great deal of research effort is now concentrated on two aspects of ferritin: its functional mechanisms and its regulation. These form the major part of the review. Steps in iron storage within ferritin molecules consist of Fe(II) oxidation, Fe(III) migration and the nucleation and growth of the iron core mineral. H-chains are important for Fe(II) oxidation and L-chains assist in core formation. Iron mobilisation, relevant to ferritin's role as iron reserve, is also discussed. Translational regulation of mammalian ferritin synthesis in response to iron and the apparent links between iron and citrate metabolism through a single molecule with dual function are described. The molecule, when binding a [4Fe-4S] cluster, is a functioning (cytoplasmic) aconitase. When cellular iron is low, loss of the [4Fe-4S] cluster allows the molecule to bind to the 5'-untranslated region (5'-UTR) of the ferritin m-RNA and thus to repress translation. In this form it is known as the iron regulatory protein (IRP) and the stem-loop RNA structure to which it binds is the iron regulatory element (IRE). **IREs** are found in the 3'-UTR of the transferrin receptor and in the 5'-UTR of erythroid aminolaevulinic acid synthase, enabling tight co-ordination between cellular iron uptake and the synthesis of ferritin and haem. Degradation of ferritin could potentially lead to an increase in toxicity due to uncontrolled release of iron. Degradation within membrane-encapsulated "secondary lysosomes' may avoid this problem and this seems to be the origin of another form of storage iron known as haemosiderin. However, in certain pathological states, massive deposits of "haemosiderin' are found which do not arise directly from ferritin breakdown. Understanding the numerous inter-relationships between the various intracellular iron complexes presents a major challenge.

L4 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:691332 CAPLUS
DOCUMENT NUMBER: 123:136107
TITLE: mRNAs containing the unstructured 5' leader sequence of alfalfa mosaic virus RNA 4 translate inefficiently in lysates from poliovirus-infected HeLa cells
AUTHOR(S): Hann, Louane E.; Gehrke, Lee
CORPORATE SOURCE: Div. Health Sci. Technol., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Virology (1995), 69(8), 4986-93
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poliovirus infection is accompanied by translational control that precludes translation of 5'-capped mRNAs and facilitates translation of the uncapped poliovirus RNA by an internal initiation mechanism. Previous reports have suggested that the capped alfalfa mosaic virus coat protein mRNA (AlMV CP RNA), which contains an unstructured 5' leader sequence, is unusual in being functionally active in exts. prepd. from poliovirus-infected HeLa cells (PI-exts.). To identify the cis-acting nucleotide elements permitting selective AlMV CP expression, the authors tested capped mRNAs contg. structured or unstructured 5' leader sequences in addn. to an mRNA contg. the poliovirus internal ribosome entry site (**IRES**). Translations were performed with PI-exts. and exts. prepd. from mock-infected HeLa cells (MI-exts.). A no. of control criteria

demonstrated that the HeLa cells were infected by poliovirus and that the exts. were translationally active. The data strongly indicate that translation of RNAs lacking an internal ribosome entry site, including AlMV CP RNA, was severely compromised in PI-exts., and find no evidence that the unstructured AlMV CP RNA 5' leader sequence acts in cis to bypass the poliovirus translational control. Nevertheless, cotranslation assays in the MI-exts. demonstrate that mRNAs contg. the unstructured AlMV CP RNA 5' untranslated region have a competitive advantage over those contg. the rabbit .alpha.-globin 5' leader. Previous reports of AlMV CP RNA translation PI-exts. likely describe inefficient expression that can be explained by residual cap-dependent initiation events, where AlMV CP RNA translation is competitive because of a diminished quant. requirement for initiation factors.

L4 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:451491 CAPLUS
DOCUMENT NUMBER: 121:51491
TITLE: Multicistronic expression units and their use in production of multimeric proteins with recombinant cells
INVENTOR(S): Dirks, Wilhelm; Wirth, Manfred; Hauser, Hansjoerg; Eichner, Wolfram; Achterberg, Volker; Doerschner, Albrecht; Meyer-Ingold, Wolfgang; Mielke, Heiko
PATENT ASSIGNEE(S): Beiersdorf A.-G., Germany; Gesellschaft fuer Biotechnologische Forschung mbH
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405785	A1	19940317	WO 1993-EP2294	19930826
W: AU, BR, CA, HU, JP, KZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4228458	A1	19940601	DE 1992-4228458	19920827
AU 9349537	A1	19940329	AU 1993-49537	19930826
EP 658198	A1	19950621	EP 1993-919176	19930826
EP 658198	B1	19990127		
R: DE, DK, ES, FR, GB, IT				
JP 08502644	T2	19960326	JP 1993-506831	19930826
ES 2127831	T3	19990501	ES 1993-919176	19930826

PRIORITY APPLN. INFO.: DE 1992-4228458 A 19920827
WO 1993-EP2294 W 19930826

AB Multicistronic expression units p-5'UTR-C1-(**IRES**-Y-C2)n-3'UTR-polyA (p-promoter; 5'- and 3'UTR=untranslated sequences preceding or following genes, resp.; C1, C2=cistrons encoding subunits of a multimeric protein, or unrelated proteins; **IRES**=internal ribosome entry sequence; Y=a sequence which, in concert with **IRES**, increases expression of C2) allow the equimolar expression of the genes located in the corresponding cistrons. These expression units are particularly suitable for the recombinant prodn. of proteins composed of 2 or more polypeptide subunits. BHK cells contg. a bicistronic plasmid were used to prep. platelet-derived growth factor AB heterodimer. The expression vector consisted of an SV40 promoter linked to the PDGF A gene, and a fragment of the Zenopus laevis .beta.-globin gene (to enhance translation) followed by a poliovirus 5'UTR (providing an **IRES**) and the PDGF B gene.

L4 ANSWER 31 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:61034 BIOSIS
DOCUMENT NUMBER: [redacted]199497074034
TITLE: Internal ribosome entry site of encephalomyocarditis virus RNA is unable to direct translation in Saccharomyces cerevisiae.
AUTHOR(S): Evstafieva, A. G. (1); Beletsky, A. V.; Borovjagin, A. V.; Bogdanov, A. A.
CORPORATE SOURCE: (1) A.N. Belozersky Inst. Physico-Chem. Biol., Moscow State Univ., 119899 Moscow Russia
SOURCE: FEBS (Federation of European Biochemical Societies) Letters, (1993) Vol. 335, No. 2, pp. 273-276. ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To evaluate the potential of the encephalomyocarditis virus (EMCV) internal ribosome entry site (**IRES**) to promote efficient expression of foreign genes in the yeast, S. cerevisiae, we have constructed E. coli-yeast shuttle vectors in which the EMCV 5' non-coding region was fused to the reporter gene, human prothymosin alpha. Efficiency of translation of corresponding RNA transcripts in mammalian cell-free systems was highly dependent on the sequence context and/or position of the initiation codon. No translation of these **IRES**-dependent mRNAs occurred in S. cerevisiae.

the cricket paralysis virus genome is an example of a naturally occurring, functionally dic cronic eukaryotic mRNA whose ti slation is controlled by two **IRES** elements located at the 5' end and in the middle of the mRNA. This finding argues that eukaryotic mRNAs can express multiple proteins not only by polyprotein processing, reinitiation and frameshifting but also by using multiple **IRES** elements.

L4 ANSWER 15 OF 31 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001137929 MEDLINE
DOCUMENT NUMBER: 20571355 PubMed ID: 11123797
TITLE: Functional characterization of the EMCV **IRES** in **plants**.
AUTHOR: Urwin P; Yi L; Martin H; Atkinson H; Gilmartin P M
CORPORATE SOURCE: Centre for Plant Sciences, Leeds Institute for Plant Biotechnology and Agriculture, University of Leeds, Leeds LS2 9JT, UK.
SOURCE: PLANT JOURNAL, (2000 Dec) 24 (5) 583-9.
Journal code: 9207397. ISSN: 0960-7412.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
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Entered Medline: 20010308

AB The translation of eukaryotic messenger RNA is typically dependent upon the presence of an m7GpppN cap structure at the 5' end of the transcript. However, several **animal** viruses, including the Picorna viruses, have been shown to exhibit cap-independent translation through the presence of an internal ribosome entry site or **IRES**. This **IRES**-mediated cap-independent internal translation initiation has been exploited to generate bicistronic transcripts that function in **animal** cells. Recently **IRES** elements have also been identified in a small number of vertebrate, **insect** and yeast cellular messenger RNAs although no such sequences have been identified in endogenous **plant** genes and there are no reports of **animal** virus derived **IRES** activity in **plant** cells. Here we have constructed a bicistronic gene containing both green fluorescent protein and luciferase open-reading frames separated by the encephalomyocarditis **IRES** element under the control of the CaMV 35S promoter. Northern analysis reveals expression of the bicistronic transcript and in vivo imaging of GFP and luciferase activities demonstrates the functional presence of both proteins. Western blot analysis confirms the independent translation of both reporter proteins. These data suggest that insertion of the encephalomyocarditis virus (EMCV) **IRES** element between two open-reading frames of a **plant** bicistronic transcript can mediate translation of the second open-reading frame. This activity is more apparent in the leaves, than in the roots, of transgenic seedlings carrying the bicistronic reporter gene construct.

L4 ANSWER 16 OF 31 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001322622 MEDLINE
DOCUMENT NUMBER: 21132877 PubMed ID: 11243410
TITLE: Inhibition of translation of mRNAs containing gamma-monomethylphosphate cap structure in frog oocytes and in mammalian cells.
AUTHOR: Chen Y; Perumal K; Reddy R
CORPORATE SOURCE: Department of Pharmacology, Baylor College of Medicine, Houston, TX 77030, USA.
CONTRACT NUMBER: GM-38320 (NIGMS)